



Pending Claims As Amended 5/22/01

29. (Twice Amended) An oligonucleotide hybridizable under stringent conditions to the nucleic acid molecule encoding on expression a leptin receptor polypeptide selected from the group consisting of:

- a. a DNA molecule of SEQ ID NO:1, 3, 5, 7, or 9;
- b. a DNA molecule complementary to the DNA molecule defined in (a);
- c. a DNA molecule which is identifiable with a polymerase chain reaction (PCR) probe selected from group consisting of a probe for clone 7 (forward primer SEQ ID NO:42 and reverse primer SEQ ID NO:43), a probe for clone 11 (forward primer SEQ ID NO:44 and reverse primer SEQ ID NO:45), and both clone 7 and clone 11; and
- d. a DNA molecule that codes on expression for the polypeptide encoded by any of the foregoing DNA molecules.

30. (Twice Amended) An oligonucleotide hybridizable under stringent conditions to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of:

- a. a leptin receptor selected from the group consisting of OB-Ra, OB-Rb, OB-Rc, OB-Rd, and OB-Re, or allelic variants thereof;
- b. a leptin receptor selected from the group consisting of:
  - i. N-terminal corresponding to OB-Ra through Lys<sup>889</sup> and C-terminal corresponding to a C-terminal selected from the group consisting of OB-Rb,

OB-Rc, and OB-Rd after Lys<sup>889</sup>;

ii. N-terminal corresponding to OB-Rb or OB-Rc through Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra or OB-Rd after Lys<sup>889</sup>;

iii. N-terminal corresponding to OB-Rd through Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra, OB-Rb, or OB-Rc after Lys<sup>889</sup>;

iv. N-terminal corresponding to SEQ ID NO:55 from Pro<sup>664</sup> to Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra, OB-Rb, OB-Rc, or OB-Rd after Lys<sup>889</sup>;

v. N-terminal corresponding to SEQ ID NO:55 from Met<sup>733</sup> to Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra, OB-Rb, OB-Rc, or OB-Rd after Lys<sup>889</sup>;

vi. N-terminal selected from the group consisting of OB-Ra, OB-Rb, OB-Rd, and SEQ ID NO:55 from Pro<sup>664</sup> through His<sup>796</sup>, and OB-Re from His<sup>796</sup>; and

vii. N-terminal corresponding to SEQ ID NO:55 from Met<sup>733</sup> to His<sup>796</sup>, and OB-Re from His<sup>796</sup>;

c. a leptin receptor wherein

- i. the N-terminal sequence is selected from the group consisting of
  - (1) amino acid residues 1-889;
  - (2) amino acid residues 23-889;
  - (3) amino acid residues 28-889;
  - (4) amino acid residues 133-889;
  - (5) amino acid residues 733-889;
  - (6) amino acid residues 1-796;

- (7) amino acid residues 23-796;
- (8) amino acid residues 28-796;
- (9) amino acid residues 28-796 preceded by an N-terminal Asp-Pro dipeptide;
- (10) amino acid residues 133-796; and
- (11) amino acid residues 733-796; and

ii. the C-terminal sequence is selected from the group consisting of

- (1) SEQ ID NO:11;
- (2) SEQ ID NO:12;
- (3) SEQ ID NO:13;
- (4) SEQ ID NO:14; and
- (5) SEQ ID NO:15 after His<sup>796</sup>;

d. a leptin receptor having an amino acid sequence selected from the group consisting of

- i. Asp-Arg-Trp-Gly-Ser-Tyr<sup>420</sup> (SEQ ID NO:77)--> Pro<sup>641</sup>;
- ii. Asp-Arg-Trp-Gly-Ser-Ser<sup>118</sup> (SEQ ID NO:78)--> Pro<sup>641</sup>;
- iii. Asp-Arg-Trp-Gly-Ser-Leu<sup>123</sup> (SEQ ID NO:79) -->Val<sup>331</sup>; and

e. a leptin receptor as described in (a)-(d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine;

wherein the numbering is based on the amino acid sequence of SEQ ID NO:55.

31. An oligonucleotide hybridizable under stringent conditions to the nucleic acid molecule

having a nucleotide sequence corresponding or complementary to the DNA sequence set forth in SEQ ID NO:1, 3, 5, 7 or 9.

32. The oligonucleotide of claim 29, 30, or 31 selected from the group consisting of SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO: 24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, and SEQ ID NO:54.

33. The oligonucleotide of claim 32 which is labeled.

67. (Amended) A method for diagnosing body weight abnormalities in a mammal comprising detecting splice variants of OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of OB-R with an oligonucleotide hybridizable under stringent conditions to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of:

a. a leptin receptor selected from the group consisting of OB-Ra, OB-Rb, OB-Rc, OB-Rd, and OB-Re, or allelic variants thereof;

b. a leptin receptor selected from the group consisting of:

i. N-terminal corresponding to OB-Ra through Lys<sup>889</sup> and C-terminal corresponding to a C-terminal selected from the group consisting of OB-Rb, OB-Rc, and OB-Rd after Lys<sup>889</sup>;

ii. N-terminal corresponding to OB-Rb or OB-Rc through Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra or OB-Rd after Lys<sup>889</sup>;

iii. N-terminal corresponding to OB-Rd through Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra, OB-Rb, or OB-Rc after Lys<sup>889</sup>;

iv. N-terminal corresponding to SEQ ID NO:55 from Pro<sup>664</sup> to Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra, OB-Rb, OB-Rc, or OB-Rd after Lys<sup>889</sup>;

v. N-terminal corresponding to SEQ ID NO:55 from Met<sup>733</sup> to Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra, OB-Rb, OB-Rc, or OB-Rd after Lys<sup>889</sup>;

vi. N-terminal selected from the group consisting of OB-Ra, OB-Rb, OB-Rd, and SEQ ID NO:55 from Pro<sup>664</sup> through His<sup>796</sup>, and OB-Re from His<sup>796</sup>; and

vii. N-terminal corresponding to SEQ ID NO:55 from Met<sup>733</sup> to His<sup>796</sup>, and OB-Re from His<sup>796</sup>;

c. a leptin receptor wherein

i. the N-terminal sequence is selected from the group consisting of

- (1) amino acid residues 1-889;
- (2) amino acid residues 23-889;
- (3) amino acid residues 28-889;
- (4) amino acid residues 133-889;
- (5) amino acid residues 733-889;
- (6) amino acid residues 1-796;
- (7) amino acid residues 23-796;
- (8) amino acid residues 28-796;
- (9) amino acid residues 28-796 preceded by an N-terminal Asp-Pro dipeptide;





- (10) amino acid residues 133-796; and
- (11) amino acid residues 733-796; and

- ii. the C-terminal sequence is selected from the group consisting of
  - (1) SEQ ID NO:11;
  - (2) SEQ ID NO:12;
  - (3) SEQ ID NO:13;
  - (4) SEQ ID NO:14; and
  - (5) SEQ ID NO:15 after His<sup>796</sup>;

d. a leptin receptor having an amino acid sequence selected from the group consisting of

- i. Asp-Arg-Trp-Gly-Ser-Tyr<sup>420</sup> (SEQ ID NO:77) -->Pro<sup>641</sup>;
- ii. Asp-Arg-Trp-Gly-Ser-Ser<sup>118</sup> (SEQ ID NO:78) -->Pro<sup>641</sup>;
- iii. Asp-Arg-Trp-Gly-Ser-Leu<sup>123</sup> (SEQ ID NO:79) -->Val<sup>331</sup>; and

e. a leptin receptor as described in (a)-(d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine;

wherein the numbering is based on the amino acid sequence of SEQ ID NO:55.

68. A method for diagnosing body weight abnormalities in a mammal comprising detecting splice variants of OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of OB-R with an oligonucleotide hybridizable under stringent conditions to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8 and 10.

69. (Amended) A method for measuring the expression of splice variants of OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of OB-R with a oligonucleotide hybridizable under stringent conditions to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of:

a. a leptin receptor selected from the group consisting of OB-Ra, OB-Rb, OB-Rc, OB-Rd, and OB-Re, or allelic variants thereof;

b. a leptin receptor selected from the group consisting of:

i. N-terminal corresponding to OB-Ra through Lys<sup>889</sup> and C-terminal corresponding to a C-terminal selected from the group consisting of OB-Rb, OB-Rc, and OB-Rd after Lys<sup>889</sup>;

ii. N-terminal corresponding to OB-Rb or OB-Rc through Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra or OB-Rd after Lys<sup>889</sup>;

iii. N-terminal corresponding to OB-Rd through Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra, OB-Rb, or OB-Rc after Lys<sup>889</sup>;

iv. N-terminal corresponding to SEQ ID NO: 55 from Pro<sup>664</sup> to Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra, OB-Rb, OB-Rc, or OB-Rd after Lys<sup>889</sup>;

v. N-terminal corresponding to SEQ ID NO:55 from Met<sup>733</sup> to Lys<sup>889</sup>, and C-terminal corresponding to OB-Ra, OB-Rb, OB-Rc, or OB-Rd after Lys<sup>889</sup>;

vi. N-terminal selected from the group consisting of OB-Ra, OB-Rb, OB-Rd, and SEQ ID NO:55 from Pro<sup>664</sup> through His<sup>796</sup>, and OB-Re from His<sup>796</sup>; and



vii. N-terminal corresponding to SEQ ID NO:55 from Met<sup>733</sup> to His<sup>796</sup>, and OB-Re from His<sup>796</sup>;



c. a leptin receptor wherein

i. the N-terminal sequence is selected from the group consisting of

- (1) amino acid residues 1-889;
- (2) amino acid residues 23-889;
- (3) amino acid residues 28-889;
- (4) amino acid residues 133-889;
- (5) amino acid residues 733-889;
- (6) amino acid residues 1-796;
- (7) amino acid residues 23-796;
- (8) amino acid residues 28-796;
- (9) amino acid residues 28-796 preceded by an N-terminal Asp-Pro dipeptide;
- (10) amino acid residues 133-796; and
- (11) amino acid residues 733-796; and

ii. the C-terminal sequence is selected from the group consisting of

- (1) SEQ ID NO:11;
- (2) SEQ ID NO:12;
- (3) SEQ ID NO:13;
- (4) SEQ ID NO:14; and
- (5) SEQ ID NO:15 after His<sup>796</sup>;

d. a leptin receptor having an amino acid sequence selected from the group consisting of

i. Asp-Arg-Trp-Gly-Ser-Tyr<sup>420</sup> (SEQ ID NO:77) -->Pro<sup>641</sup>;



- ii. Asp-Arg-Trp-Gly-Ser-Ser<sup>118</sup> (SEQ ID NO:78) -->Pro<sup>641</sup>;
- iii.. Asp-Arg-Trp-Gly-Ser-Leu<sup>123</sup> (SEQ ID NO:79) -->Val<sup>331</sup>; and

e. a leptin receptor as described in (a)-(d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine;

wherein the numbering is based on the amino acid sequence of SEQ ID NO:55.

70. A method for measuring the expression of splice variants of OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of OB-R with a oligonucleotide hybridizable under stringent conditions to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8 and 10.

71. The method of any of claims 67-70 wherein the oligonucleotide is labeled.

72. The method of any of claims 67-70 wherein the nucleic acid molecule is RNA.

73. The method of any claims 67-70 wherein the oligonucleotide is selected from the group consisting of SEQ ID NO: 20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54.